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(54) Dialysis fluids

(57) Peritoneal dialysis fluid contains as active ingredient for inhibiting growth of bacteria a non-toxic iron-chelation substance e.g. transferrin or lactoferrin of concentration about 20μM.

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FIG. 1. Effect of transferrin on the growth of Staphyloccocus epidermidis in P.D. effluent supplemented with 10 μM ferric chloride.

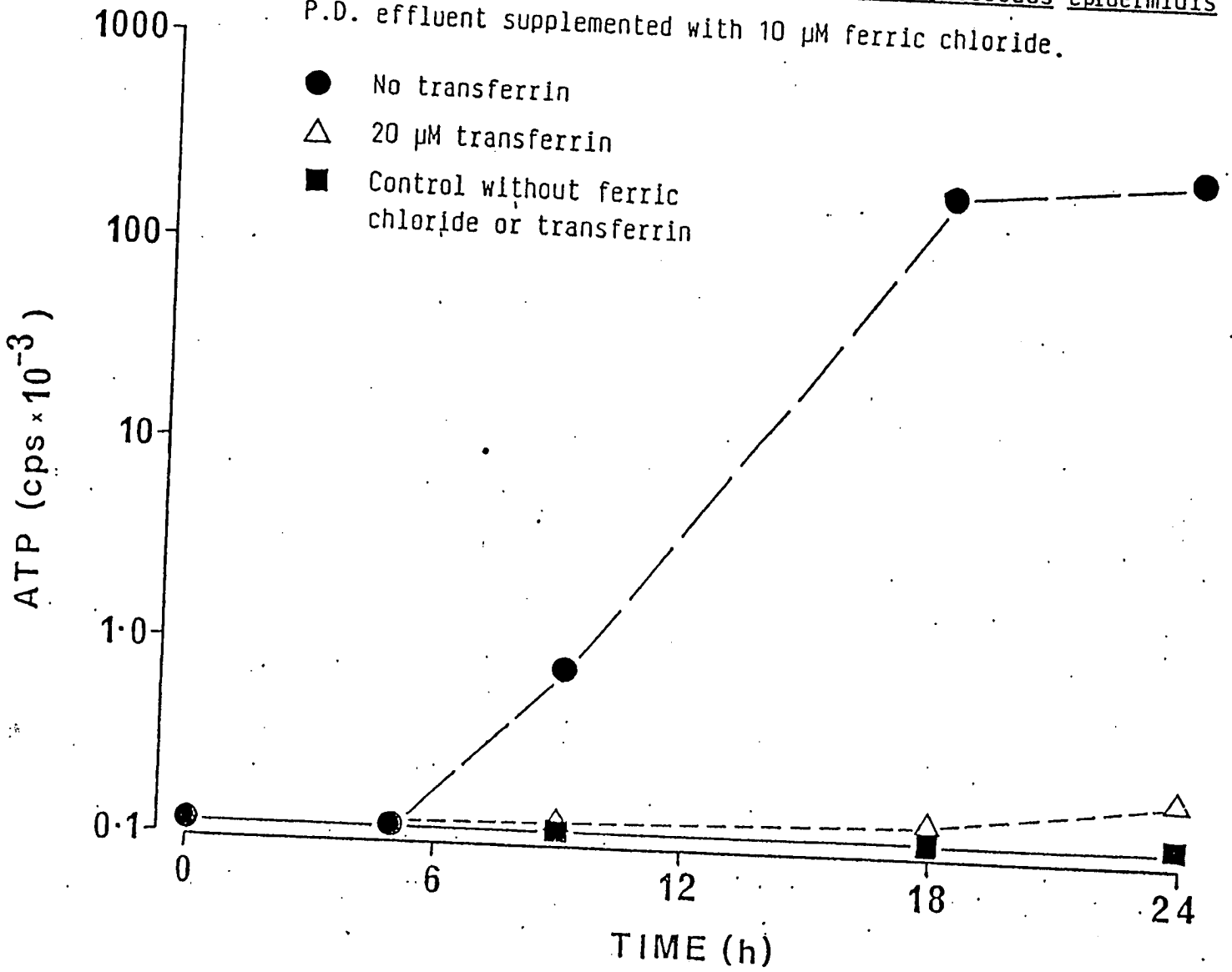
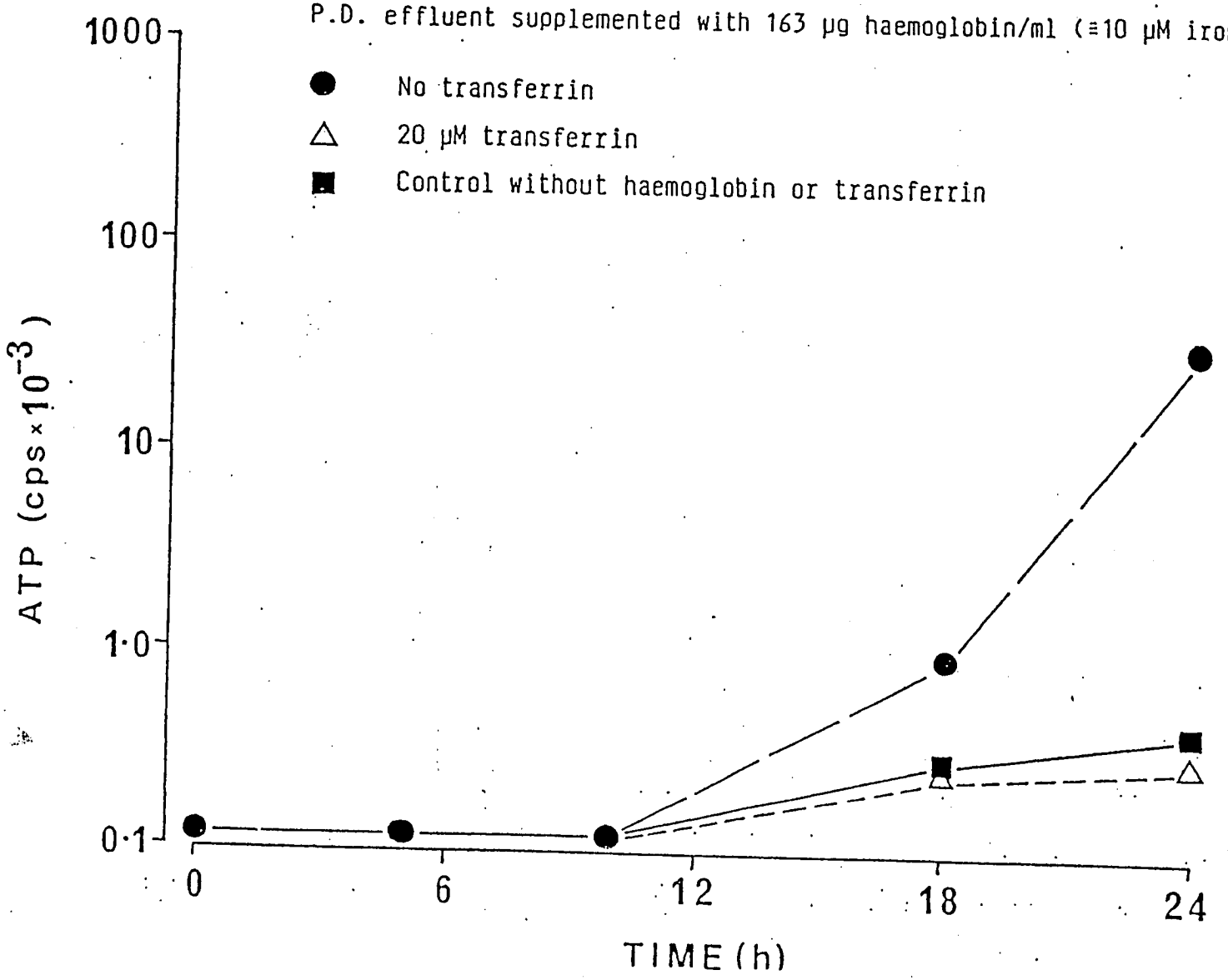
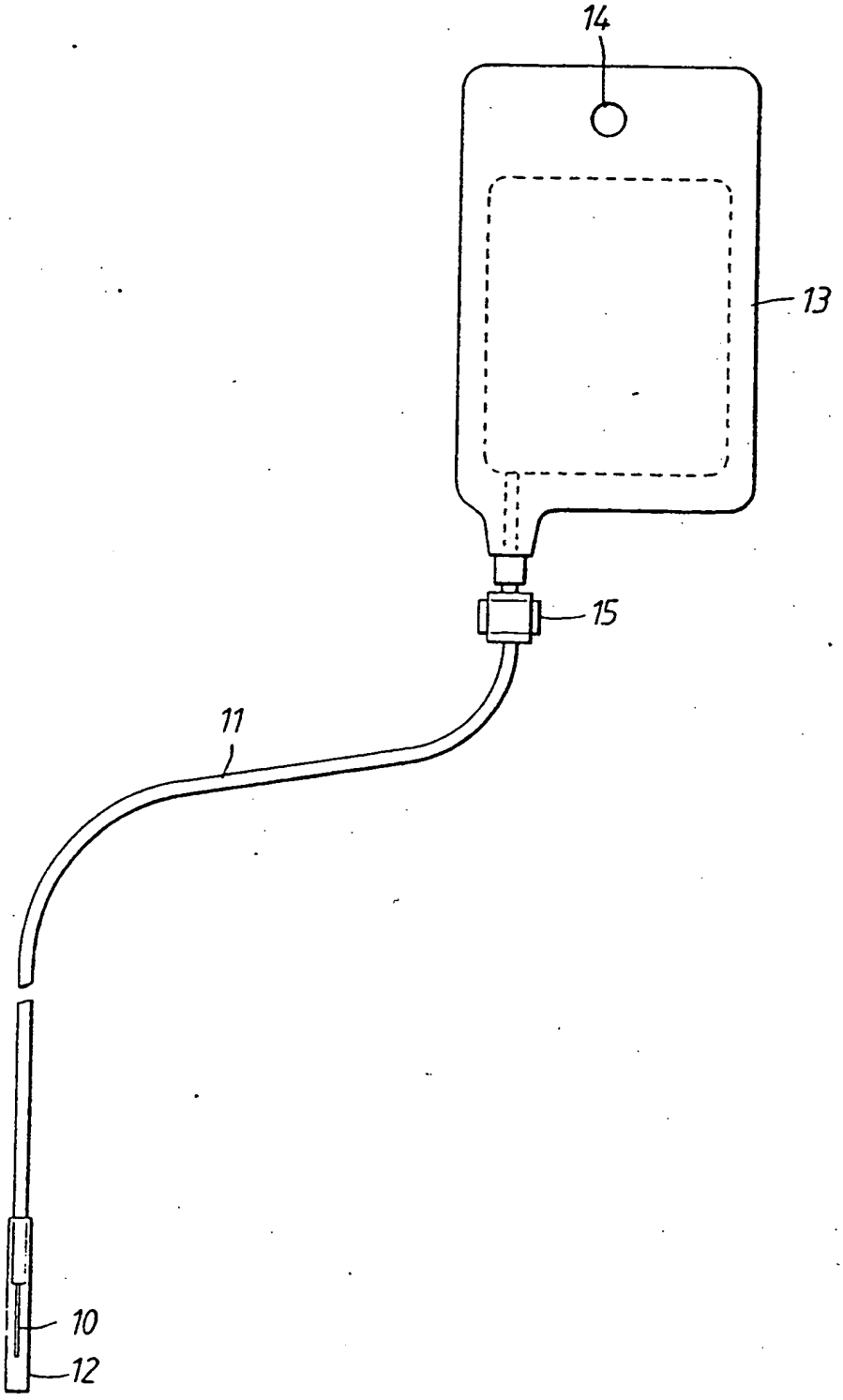


FIG. 2. Effect of transferrin on the growth of Staphylococcus epidermidis in P.D. effluent supplemented with 163 µg haemoglobin/ml (≡10 µM iron).





SPECIFICATION

Dialysis fluids

Peritoneal dialysis (PD) is an important method for treating patients with end-stage renal failure, and the development of continuous ambulatory peritoneal dialysis (CAPD) has become increasingly popular within the last decade. The major problem with these techniques is bacterial growth in the dialysate fluid resulting in peritonitis. A method for preventing, or even delaying, bacterial growth in PD fluids *in vivo* would represent a major clinical advance.

All bacteria require iron as a nutrient for growth, but because most of the body iron is tightly bound to host proteins its availability is usually the rate-limiting factor for bacterial growth *in vivo*. We have shown that addition of iron to dialysis effluent obtained from patients undergoing PD, either in the form of ferric chloride or as haemoglobin, greatly enhances the capacity of the effluent to support rapid bacterial growth. Conversely, supplementation of the iron-rich effluent with the human iron-binding protein transferrin was found to have a profound inhibitory effect on the growth rate of common peritoneal pathogens. These observations suggest that transferrin, or any other non-toxic iron-chelating agent, could be of great value in preventing peritonitis if routinely incorporated into PD fluids.

Broadly stated the invention consists in a dialysis fluid including a non-toxic iron-chelation substance.

The iron-chelation substance may comprise the human proteins transferrin or lactoferrin, or it could be a non-protein iron-chelator. The chelator is preferably present at a concentration of between 5 and 50μM and preferably about 20μM.

From another aspect the invention consists in a method of treating a patient by peritoneal dialysis using a dialysis fluid as defined above.

Experimental

Four bacterial strains were selected for study: *Staphylococcus epidermidis, Escherichia coli, Pseudomonas aeruginosa* and *Proteus mirabilis*. Peritoneal dialysis effluent was obtained from four patients with peritonitis and a pool was prepared which was supplemented with either ferric chloride (10 μM) or haemoglobin (163 μg/ml ≡ 10 μM iron). Some samples were also supplemented with human transferrin at a concentration of 5, 20, or 50 μM. These and control samples in 5ml volumes were inoculated with each of the test organisms to give an initial bacterial count of about 4×10^3 colony-forming units/ml, and they were then incubated in a waterbath at 37° C for 24 h. Bacterial growth was accessed by withdrawing 100 μl aliquots at regular intervals and measuring extractable adenosine triphosphate (ATP) using the firefly bi luminescence assay.

Transferrin strongly inhibited the growth of all four baterial strains in PD effluent supplemented with ferric chloride, and also produced a significant suppression of bacterial growth rate in PD effluent supplement d with haemoglobin. Results obtained using the strain of *S.epidermidis*, the most common peritoneal pathogen, are presented in Figures 1 and 2.

In performing the peritoneal dialysis a quantity of sterile dialysis fluid, usually about two litres and containing various salts, glucose and lactate, with the iron-chelator as specified, will be introduced into the peritoneal cavity via a catheter which is usually left in situ. An exchange occurs between the constituents of the fluid and the waste products in the blood stream (urea, creatinine etc.) across the peritoneum. The effluent is withdrawn after several hours and replaced with fresh fluid. It is usual for a patient to have four such exchanges per day.

The equipment needed for performing the invention is illustrated in the accompanying drawing: it comprises a catheter needle 10 attached to a flexible feed tube 11 and initially protected by a sterile cap 12, the tube being attached to a fluid container 13 having a suspention tab or opening 14 at its upper end and a control valve 15 at the lower end. The fluid container 13 is initially filled with the dialysis fluid, as described above, and the fluid is introduced into the patient's peritoneal cavity via the catheter, simply by holding the container above the level of the catheter and opening the valve 15. After the predetermined period of time the container is lowered and the valve is again opened and as a result the effluent is discharged from the cavity back into the container. Instead of a static dialysis system as described the invention may be used with a portable continuous ambulatory dialysis machine designed to be carried by the patient or worn in the clothing.

CLAIMS

1. A dialysis fluid including a non-toxic iron-chelation substance.
2. A dialysis fluid according to Claim 1, in which the iron-chelation substance is a protein.
3. A dialysis fluid according to Claim 2, in which the iron-chelation substance is human transferring or lactoferrin.
4. A dialysis fluid according to any of the preceding claims, in which the chelator is present at a concentration of between 5 and 50μM and preferably about 20μM.
5. A method of operating a dialysis machine for peritoneal dialysis, using a dialysis fluid according to any of the preceding claims.
6. A dialysis machine operating with a dialysis fluid according to any of Claims 1 - 4.

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